REMARKS

Applicants appreciate the Examiner's thorough examination of the subject application and request reconsideration of the subject application based on the foregoing amendments and the following remarks.

Claims 20-29, 31-41, 48-50, 58 and 59 are pending in the subject application.

Claims 20-29, 31-41, 48-50, 58 and 59 stand rejected under 35 U.S.C. §103.

35 U.S.C. §103 REJECTIONS

Motamedi and Swanson

Claims 20, 21, 24-29, 31, 32, 37-41, 48-50, 58 and 59 are rejected over Motamedi et al. [USP 6,143,019; "Motamedi"] in view of Swanson [USP 6,023,638; "Swanson"] for the reasons provided on page 2 of the above referenced Office Action. Applicants respectfully traverse.

Applicants claim, claim 20, a non-thermal method for treating and/or curing cardiac arrhythmias. According to Applicants' method, a photosensitizing agent is administered to a desired treatment site, a device having an illumination mechanism is positioned so the illumination mechanism is spaced from the surface of the treatment site such that radiation emitted by the illuminating mechanism impinges upon the surface, and the device is used to destroy tissues and pathways from which abnormal signals arise and/or in other cardiac tissues by photochemotherapy or photodynamic therapy using the administered photosensitizing agent. By destroying the tissues and pathways, abnormal electrical rhythms cannot be generated and/or sustained. Applicants' method utilizes MR imaging to guide the device and assist in monitoring the progress of the photochemotherapy or photodynamic therapy.

Applicants' claim 26 is similar to claim 20, and adds that device is positioned so the illumination mechanism is spaced from the surface of a treatment site of the pulmonary vein such that radiation emitted by the illuminating mechanism impinges upon the surface.

Applicants claim, claim 21, a method for treating and/or curing cardiac arrhythmias using photochemotherapy or photodynamic therapy. According to Applicants' method, a device is provided comprising an illumination mechanism and an MRI receiver. A photosensitizing agent is administered to a desired treatment site. The device is positioned proximal the desired treatment site using MRI to guide the device, and the illuminating mechanism is arranged so as to be spaced from a surface of the treatment site. Laser energy is delivered at a wavelength required to activate the photosensitizing agent, and MR imaging is used to assist in monitoring the progress of the photochemotherapy or photodynamic therapy.

Applicants claim, claim 27, a method to treat and/or cure cardiac arrhythmias using photochemotherapy or photodynamic therapy. According to the method, a therapeutically effective amount of a photosensitizing agent is delivered to the cardiac tissue, and the photosensitizing agent is preferentially absorbed by the tissues and pathways from which abnormal signals causing the arrhythmias arise. An illumination mechanism is positioned so it is spaced from a surface of the treatment site of the cardiac tissue such that radiation emitted by the illuminating mechanism impinges upon the surface. The photosensitizing agent is then activated with the illumination mechanism, and MR imaging is used to guide and monitor the treatment.

Motamedi describes a method for delivering ablating energy within myocardial tissue. According to Motamedi, heating and coagulating myocardial tissues responsible for cardiac arrhythmias is of great therapeutic value (col. 1, lines 29-32). However, as pointed out by Motamedi, previous instruments for heating such tissues were inadequate because the ablation "tip does not directly reach deep intramyocardial tisuse where arrhythmias may arise" and are "inadequate for ablating such deep tissue" (col. 1, lines 57-62). To overcome these inadequacies, Motamedi developed a device and method for "directly heating the heart" (col. 2, lines 33-34) by "intramyocardial delivery of diffused laser light, or other ablating energy" (col. 2, lines 55-56). Motamedi's method requires, "extending the distal end of the conductor past the distal end of the

catheter and into the tissue, and transmitting ablating energy through the conductor into the tissue" (col. 3, line 67-col 4, line 3). As set out, "When the distal end 24 of the catheter 22 is in the desired position, the tip 42 * * * is extended past the sheath 36 a predetermined distance, puncturing the endocardium 30 and extending 62 into the myocardial tissue 32" (col. 8, lines 28-32).

Thus, Motamedi addresses a specific problem and solves the problem by extending the energy transmitting tip into the tissue being treated so that the tissue can be directly heated. Motamedi does not teach or suggest a method wherein an illumination mechanism is spaced from the surface of the treatment site such that radiation emitted by the illuminating mechanism impinges upon the surface as set out in Applicants' claims 20, 21, 26, and 27. Rather, Motamedi specifically teaches away from such treatment because, according to Motamedi, such methods are inadequate for ablating such deep tissue, which is the goal of Motamedi.

Applicants point out that Motamedi is directed to method for heating the heart. Throughout the disclosure, Motamedi discussing such thermal heating and thermal ablation of tissues. For example, according to Motamedi, "In the practice of the method, devices emitting laser, ultrasound, microwave, radiofrequency or conductive heat as from a hot tip may be used to heat the heart tissue." (col. 4, lines 37-39) Motamedi specifically defines "ablate" as "thermally coagulate and/or remove the tissues * * * and in a more general sense, ablation means the desiccation of tissue by the application of heat." Further, "ablating energy would be one that would cause the tissue to reach a temperature of at least 80-90°C." (col. 5, lines 55-61) Motamedi mentions photodynamic therapy (col. 6, lines 1-5) but sets forth no guidance as to how such a method could be carried out. Applicants, on the other hand, teach methods wherein photochemotherapy or photodynamic therapy is used to destroy the tissues and pathways from which abnormal signals arise. In one embodiment, photochemotherapy or photodynamic therapy is used to ablate at least a section of the pulmonary vein to electrically isolate the pulmonary vein from the left atrium. This is done by positioning the device within the vein and emitting a light

outwards to the surface of the vein so as to activating photosensitizing agent delivered to the vein. Applicants' methods do not rely on thermal conduction, which results in regions of graded tissue injury. Rather, Applicants utilize photochemotherapy to create continuous and uniform lesions by providing uniform illumination within the region of ablation, as opposed to uniform heating which is the goal set forth by Motamedi.

In view of the above, Applicants respectfully submit that Motamedi is directed to a very different method than that taught by Applicants. Applicants teach a method wherein an illumination source is spaced from the surface of the treatment site such that radiation emitted by the illuminating mechanism impinges upon the surface. An administered photosensitizing agent, which is delivered to the tissue of the treatment site, is activated by the radiation and destroys the tissue. Motamedi, on the other hand, describes a method wherein tissues of the heart are directly heated by extending the tip of the catheter into the tissue and transmitting energy directly into the tissue. Motamedi teaches away from spacing the tip of the catheter from the tissue due to alleged inadequacies of such methods. Motamedi further focuses on thermal tissue destruction and does not set forth any guidance regarding methods for photodynamic therapy other than mentioning that it could be an alternative to the thermal methods. Still further, Motamedi does not teach or suggest utilizing MR imaging to guide the device and assist in monitoring the progress of the therapy.

Swanson does not remedy the above-noted deficiencies of Motamedi. Swanson describes a system and method for temporarily stunning a zone of tissue, temporarily rendering it electrically unresponsive (Abstract). This is a diagnostic testing method that enables a physician to easily identify the tissue that is intended for modification as well as tissue that is not (col. 3, lines 54-65). In some embodiments, a common electrode is used to both temporarily render tissue unresponsive as well as modify the tissue by varying the energy applied to the tissues. The amount of energy applied by the common electrode is modified so as to either stun or modify the tissue as desired. Thus, Swanson does not teach photochemotherapy or photodynamic therapy to

destroy tissues, but, rather, specifically teaches application of RF energy to thermally stun and modify tissue by use of a common electrode. Further, Swanson teaches methods wherein the splines 30, which carry an array of electrodes 24 bend to conform to the endocardial tissue surface they contact and, thus, the electrodes are placed in contact with the tissues (see, e.g. col. 7, lines 57-61, col. 18, lines 15-19; col. 18, lines 53-55).

Further, Motamedi and Swanson do not teach a method wherein the device is positioned so the illumination mechanism is spaced from the surface of a treatment site of the pulmonary vein such that radiation emitted by the illuminating mechanism impinges upon the surface, as set forth in claim 26.

Thus, claims 20 and 21, 26, and 27 are patentable over Motamedi and Swanson. Claims 28, 29, 31-41, 48-50, 58 and 59 depend from claims 20, 21, 26, and 27 and, likewise, are patentable over Motamedi and Swanson. Reconsideration and withdrawal of the rejection is respectfully requested.

Motamedi, Swanson and Altman

Claims 22 and 23 are rejected under 35 U.S.C. 103(a) over Motamedi and Swanson, as applied to claims 20, 21, 24-29, 31, 32, 37-41, 48-50, 58, and 59 above, and Altman.

Applicants respectfully traverse.

Applicants claim, claim 22, a method to electrically isolate the pulmonary vein from the left atrium comprising the steps of using photochemotherapy or photodynamic therapy to electrically isolate the pulmonary vein from the left atrium under the guidance of MR imaging.

As set forth above, Motamedi describes a method wherein ablating energy is delivered *within myocardial tissue*. Motamedi is specifically focused on heating and coagulating

myocardial tissues responsible for cardiac arrhythmias. Motamedi points out that previous instruments for heating such tissues were inadequate because the ablation "tip does not directly reach deep intramyocardial tisuse where arrhythmias may arise" and are "inadequate for ablating such deep tissue" (col. 1, lines 57-62). Thus, Motamedi's device and method overcomes these inadequacies by providing "intramyocardial delivery of diffused laser light, or other ablating energy" (col. 2, lines 55-56) to directly heat the heart (col. 2, lines 33-34). Motamedi accomplishes this by "extending the distal end of the conductor past the distal end of the catheter and *into the tissue,* and transmitting ablating energy through the conductor *into the tissue*" (col. 3, line 67-col 4, line 3).

Motamedi does not teach or suggest a method wherein the pulmonary vein is electrically isolated from the left atrium. Rather, Motamedi only describes ablating myocardial tissue (the muscular tissue of the heart). Further, as set out above, Motamedi's methods and devices are directed to thermally heating the heart. Motamedi merely mentions photodynamic therapy (col. 6, lines 1-5) as an alternate to thermal heating, but sets forth no guidance as to how such a method could be carried out.

As set forth above, Swanson does not teach photochemotherapy or photodynamic therapy to destroy tissues, but, rather, specifically teaches application of RF energy to thermally stun and modify tissue by use of a common electrode.

Altman describes a diagnostic medical device and method whereby it can be diagnosed whether ablation of a portion of the pulmonary vein will eliminate atrial fibrillation originating in the pulmonary vein. According to Altman, a fluid is administered to the target pulmonary vein, and the fluid temporarily inhibit electrical impulses in the target pulmonary vein. Altman's, thus, describes a purely diagnostic procedure. Altman does not teach or suggest a method of using photochemotherapy or photodynamic therapy to electrically isolate the pulmonary vein from the left atrium under the guidance of MR imaging.

Applicants respectfully submit that claim 22 is patentable over Motamedi, Swanson, and Altman. There is no suggestion or motivation to modify the references or to combine the references. Further, Motamedi, Swanson, and Altman, alone and in combination, fail to teach or suggest and every element of claim 22. Motamedi describes a process wherein a thermal energy conductor is inserted into myocardial tissue and the tissue heated directly by the conductor. There is no teaching or suggestion to apply any of Motamedi's methods to pulmonary veins, and there would be no reasonable expectation of success in doing so. Rather, Motamedi's device and method is directed to heating deep intramyocardial tisuse where arrhythmias arise and coagulating these tissues. Motamedi does not teach or suggest how or if phytodynamic therapy may be used to electrically isolate the pulmonary vein from the left atrium. Swanson describes a diagnostic process wherein electrodes are placed in contact with tissue and energy applied to the tissue to temporarily stun the tissue. The energy applied by the electrodes may be altered so as to modify the tissue in some embodiments. Swanson does not teach or suggest how or if phytodynamic therapy may be used to electrically isolate the pulmonary vein from the left atrium. Altman describes a diagnostic method wherein fluid is delivered to the pulmonary vein to temporarily inhibit electrical impulses, thereby allowing a physician to determine whether the target site is where the atrial fibrillation is triggered. Altman does not teach or suggest how or if phytodynamic therapy may be used to electrically isolate the pulmonary vein from the left atrium.

Accordingly, Applicants respectfully submit that claim 22 is patentable over Motamedi, Swanson, and Altman. Reconsideration and withdrawal of the rejection is respectfully requested.

Applicants claim, claim 23, a method of ablating at least a section of the pulmonary vein using photochemotherapy or photodynamic therapy, comprising the steps of using a device to ablate at least a section of the pulmonary vein, and using MR imaging to monitor the progress of

the ablation. According to Applicants' method, the device is positioned so the illumination mechanism thereof is spaced from the surface of a treatment site of the pulmonary vein such that radiation emitted by the illuminating mechanism impinges upon the surface.

Applicants respectfully traverse for the reasons set forth above regarding claim 22. Further, as set forth above in relation to claims 20 and 21, 26, and 27, Motamedi and Swanson do not teach or suggest a method wherein the device is positioned so the illumination mechanism thereof is spaced from the surface of a treatment site of the pulmonary vein such that radiation emitted by the illuminating mechanism impinges upon the surface. Rather, Motamedi requires insertion of the conductor within the myocardial tissue treated. Swanson describes a method wherein the device bends to conform to the tissue surface such that the electrodes are placed in contact with the tissues and thermal energy applied by the conductor is applied to the tissue. Altman does not teach or suggest a method utilizing an illumination or energy source or positioning such a source spaced from the surface of a treatment site. As set out, Altman does not teach devices or methods for treating tissue, but, rather, describes a diagnostic device and method for determining where atrial fibrillation is triggered.

Accordingly, claim 23 is patentable over Motamedi, Swanson, and Altman. Reconsideration and withdrawal of the rejection is respectfully requested.

Motamedi, Swanson, and Leone

Claims 33-36 are rejected under 35 U.S.C. 103(a) over Motamedi and Swanson as applied to claims 20, 21, 24-29, 21, 32, 37-41, 48-50, 58, and 59 and Leone.

Applicants respectfully traverse.

Claims 33-36 depend from claims 21 and 27. As set forth above regarding claims 21 and 27, Motamedi and Swenson, alone and in combination, fail to teach or suggest a method for

treating and/or curing cardiac arrhythmias using photochemotherapy or photodynamic therapy wherein a photosensitizing agent is administered to a desired treatment site, a device with an illuminating mechanism is positioned using MRI to guide the device such that the illuminating mechanism is spaced from a surface of the treatment site such that radiation emitted by the illuminating mechanism impinges upon the surface, and delivering laser energy at a wavelength required to activate the photosensitizing agent. Leone does not remedy these deficiencies. Leone describes a photodynamic therapy balloon catheter. Leone does not teach or suggest a method for treating and/or curing cardiac arrhythmias using photochemotherapy or photodynamic therapy by administering a photosensitizing agent, positioning a device with an illuminating mechanism using MRI to guide the device such that the illuminating mechanism is spaced from a surface of the treatment site and such that radiation emitted by the illuminating mechanism impinges upon the surface, and delivering laser energy at a wavelength required to activate the photosensitizing agent.

Accordingly, claims 21 and 27 are patentable over Motamedi, Swanson, and Leone. Claims 33-36 depend from claims 21 and 27 and, likewise, are patentable over Motamedi, Swanson, and Leone. Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicant respectfully requests early consideration and allowance of the subject application.

Applicants believe that additional fees are not required in connection with the consideration of the within matter. However, if for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105.**

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

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Respectfully submitted,

By _____

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